**PATENT** 

PETER ALAN HUNT, et al. Application No.: 09/647,054 Page 2

 $\begin{array}{c|c}
Q^{2} & Q^{3} \\
Q^{1} & Q^{3} \\
R^{N} & M' & R^{C}
\end{array}$ 

wherein:-

w indicates a bond at a chiral centre of the structure which centre may be in the R or S configuration or a mixture thereof;

R and R<sup>2</sup> is an amino acid side chain group which may be the same or different;

M<sup>I</sup> and M<sup>II</sup> may be the same or different and are selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, chloro and C<sub>1</sub>-C<sub>4</sub> alkoxy;

 $R^N$  is  $-N(Z^I)Pg^N$  where  $Z^I$  is selected from the group consisting of hydrogen, methyl and part of a cyclic amino acid sidechain joined to  $Q^I$ , and PgN is a protecting group for amine;

R<sup>C</sup> is selected from the group consisting of a carboxy terminal part of the mimetic, hydrogen, R, and -CH<sub>2</sub>R;

 $Q_1 = R^1$  which has the same definition as R and  $R^2$  above and  $Q^2 = Z$  where Z is selected from the group consisting of hydrogen, methyl, ethyl, formyl and acetyl, -CH<sub>2</sub>R, and -C(O)R or alternatively Z is part of a cyclic amino acid side chain group joined to  $R^2$ ; or  $Q^1$  and  $Q^2$  taken together represent a cyclic group;

 $Q^3$  is selected from the group consisting of Y, C(O)NHCH(R)Y-, - C(O)ENHCH(R)Y-, - $C(O)N(Q^5)CH(R)Y$ - wherein Y is selected from the group consisting of C(O) and  $CH_2$  and  $Q^5$  is a covalent bond from the  $Q^4$  group to the nitrogen atom in  $Q^3$  to form a bicyclic ring system or alternatively, is selected from the group consisting of hydrogen,  $C_1$ - $C_4$  alkyl, chloro and  $C_1$ - $C_4$  alkoxy and E is  $(AA)_n$  where n is 1-300 and AA is an amino acid residue; and



 $Q^4$  is selected from the group consisting of CH(M<sup>1</sup>), C(O), CH(Q<sup>5</sup>)CH<sub>2</sub> and CH(Q<sup>5</sup>) C(O),

with the provisos that when:-

- (i)  $\sqrt{Q^4} = CH(M^1)$ , Y is C(O);
- (ii)  $Q^4 = C(O)$ , Y is CH<sub>2</sub>;
- (iii)  $Q^4 = CH(Q^5)CH_2$ , Y is C(O);
- (iv)  $Q^4 \stackrel{\searrow}{=} CH(Q^5)C(O)$ , Y is  $CH_2$ ; and
- (v)  $Q^3 = -C(O)N(Q^5)CH(R)Y$ ,  $Q^5$  is a covalent bond from the  $Q^4$  group to the nitrogen atom in  $Q^3$  which is a cyclization forming a bicyclic ring system.
- 75. A peptide mimetic as claimed in claim 74 wherein when  $Q_1$  and  $Q_2$  form a cyclic group,  $Q_1Q_2$  is selected from the group consisting of -CH(R)C(O)-, -

 $CH_2CH(R)C(O)$ -,  $-CH_2CH_2CH(R)C(O)$ -

-CH(R)CH<sub>2</sub>-, -CH<sub>2</sub>CH(R)CH<sub>2</sub>-, -CH<sub>2</sub>CH(R)CH<sub>2</sub>-, -CH<sub>2</sub>CH(R)-,

-CH<sub>2</sub>CH<sub>2</sub>CH(R)-, -CH(R)CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH(R)CH<sub>2</sub>CH<sub>2</sub>-,

-CH(R)CH<sub>2</sub>C(O)- and -CH<sub>2</sub>CH(R)CH<sub>2</sub>C( $\phi$ )

- 76. A peptide mimetic as claimed in Claim 74 wherein n is 1-30.
- 77. A peptide mimetic as claimed in Claim 74 wherein E represents a loop of n amino acids which additionally incorporate non-alpha amino acid(s), alpha dialkyl amino acid(s) or other amino acid which provides the peptide mimetic with increased binding affinity or increased ease of detection, identification or purification.
  - 78. A peptide mimetic as claimed in Claim 74 wherein  $Q^1$  is R,  $Q^2$  is Z,  $Q^3$  is Y.
- 79. A peptide mimetic as claimed in Claim 74 wherein  $Q^1$  is R,  $Q^2$  is Z,  $Q^3$  is C(O)NHCH(R)Y and  $Q^5$  is  $M^1$ .
- 80. A peptide mimetic as claimed in Claim 74 wherein  $Q^1$  is R,  $Q^2$  is Z,  $Q^3$  is C(O)NHCH(R)C(O)-NHCH(R)Y and  $Q^5$  is  $M^1$ .
- 81. A peptide mimetic as claimed in Claim 74 wherein  $Q^1$  is R,  $Q^2$  is Z,  $Q^3$  is  $C(O)N(Q^5)CH(R)Y$  and  $Q^5$  is a covalent bond to  $Q^3$ .

CONT.

82. A peptide mimetic as claimed in Claim 74 wherein  $Q^1$  is  $CH(R)C(O)Q^2$ ,  $Q^2$  is a covalent bond to  $Q^1$ ,  $Q^3$  is Y and  $Q^5$  is  $M^1$ .

83. A peptide mimetic as claimed in Claim 74 wherein  $Q^1$  is  $CH_2CH(R)C(O)Q^2$ ,  $Q^2$  is  $Q^1$ ,  $Q^3$  is X and  $Q^5$  is  $M^1$ .

84. A peptide mimetic as claimed in Claim 74 wherein R<sup>C</sup> is C(O)Pg<sup>C</sup> where Pg<sup>C</sup> is a protecting group for carboxylic acid.

85. A peptide mimetic as claimed in Claim 84 wherein Pg<sup>C</sup> is selected from the group consisting of alkoxy, benzyloxy, allyloxy, fluorenyl methyloxy, amines forming easily removable amides, a cleavable linker to a solid support, the solid support itself, hydroxy-NHR, C(O)R and the remaining C-terminal portion of the mimetic.

86. A peptide mimetic as claimed in Claim 85 wherein PgC is methoxy or ethoxy.

87. A peptide mimetic as claimed in Claim 74 wherein Pg<sup>N</sup> is a protecting group for an amine.

88. A peptide mimetic as claimed in Claim 74 wherein Pg<sup>N</sup> is selected from the group consisting of Boc, Cbz, Fmoc, Alloc, trityl, a cleavable linker to a solid support, the solid support itself, hydrogen, R, C(O)R and the remaining N terminal portion of the mimetic.

89. A peptide mimetic as claimed in Claim 74 wherein M<sup>I</sup> or M<sup>II</sup> is methoxy.

90. A peptide mimetic as claimed in Claim 4 wherein M<sup>I</sup> or M<sup>II</sup> is methyl.

91. Compounds I(i)a having the structure:

wherein R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are amino acid side chain groups, Pg<sup>N</sup> is a protecting group for amino, Pg<sup>C</sup> is a protecting group for carboxylic acid and M indicates



Page 5

a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

92. Compounds I(i)a as claimed in Claim 91 where  $R_1$  and  $R_2 \neq H$ .

93. Compounds I(ii)a having the structure:

wherein R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are amino acid side chain groups, Pg<sup>N</sup> is a protecting group for amino, Pg<sup>C</sup> is a protecting group for carboxylic acid and M indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

94. Compounds I(ii)a as claimed in Claim 93 where  $R_1$  and  $R_2 \neq H$ .

95. Compounds II(i)a having the structure:

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and m indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

- 96. Compounds II(i)a as claimed in Claim 95 where  $R_1$  and  $R_2 \neq H$ .
- 97. Compounds II(iii)a having the structure:



Page 6

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and m indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

- 98. Compounds II(iii)a as claimed in Claim 97 where  $R_1$  and  $R_2 \neq H$ .
- 99. Compounds III(i)a having the structure:

wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R^5$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and M indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

100. Compounds III(iii)a having the structure:



Page 7

III(iii)a

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and  $R^5$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and m indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

# 101. Compounds IV(i)a having the structure:

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and m indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

### 102. Compounds IV(ii)a having the structure:



Page 8

$$R^2$$
 $HN$ 
 $R^4$ 
 $R^1$ 
 $R^1$ 
 $R^1$ 
 $R^2$ 
 $R^4$ 
 $R^4$ 
 $R^1$ 
 $R^4$ 
 $R^1$ 
 $R^2$ 
 $R^4$ 
 $R^4$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^7$ 
 $R^4$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^6$ 
 $R^7$ 
 $R^6$ 
 $R^6$ 

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and  $\infty$  indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

### 103. Compounds V(i)a having the structure:

$$R^2$$
 $N$ 
 $R^3$ 
 $R^4$ 
 $R^1$ 
 $Pg^N$ 
 $O$ 
 $Pg^C$ 
 $V(i)a$ 

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino,  $Pg^C$  is a protecting group for carboxylic acid and m indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

## 104. Compounds V(ii)a having the structure:

V(ii)a

Page 9

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino, Pg<sup>C</sup> is a protecting group for carboxylic acid and M indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

#### 105. Compounds VI(i)a having the structure:

wherein  $R_1$ ,  $R_2$   $R_3$  and  $R^4$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino, Pg<sup>C</sup> is a protecting group for carboxylic acid and M indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

### 106. Compounds VI(ii)a having the structure:

 $\mbox{VI(ii)a}$  wherein  $R_1,\,R_2\,\,R_3$  and  $\mbox{R}^4$  are amino acid side chain groups,  $\mbox{Pg}^N$  is a protecting group for amino, Pg<sup>C</sup> is a protecting group for carboxylic acid and № indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof.

107. A process for making mimetics I(i)a having the structure:



Page 10

wherein  $R^1$ ,  $R^2$  and  $R^3$  are amino acid side chain groups,  $Pg^N$  is a protecting group for amino and  $Pg^C$  is a protecting group for carboxylic acid and m indicates a bond at a chiral center of the structure which centre may be in the R or S configuration or a mixture thereof wherein compounds having the structure:

are reacted with vinyl magnesium bromide to form compounds having the

structure:

which are then reacted with compounds having the structure:

to form compounds having the structure:

which are then reacted with compounds having the structure:

